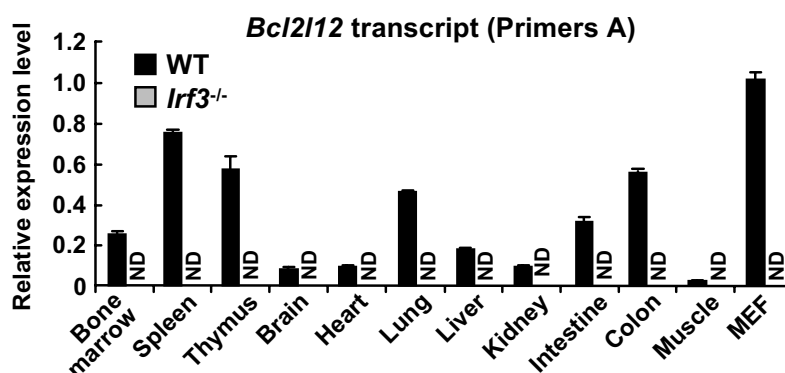


# Supporting Information

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**Fig. S1.** qRT-PCR for the *Bcl2l12* transcript in various tissues from WT and *Irf3*<sup>-/-</sup> *Bcl2l12*<sup>-/-</sup> mice. Primers A detect the 18th to 63rd nucleotides from the AUG of the WT *Bcl2l12* mRNA. ND, not detectable.

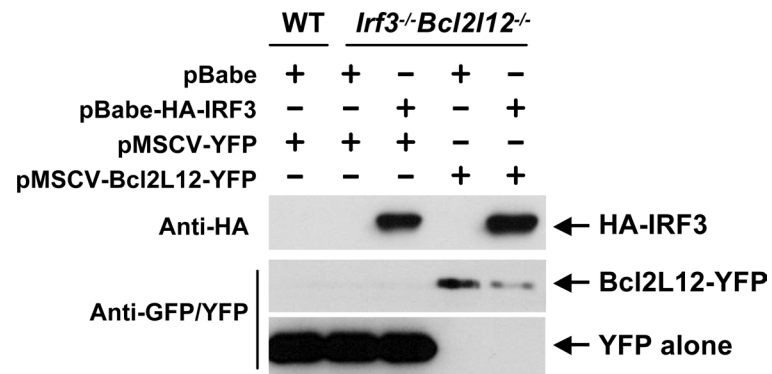
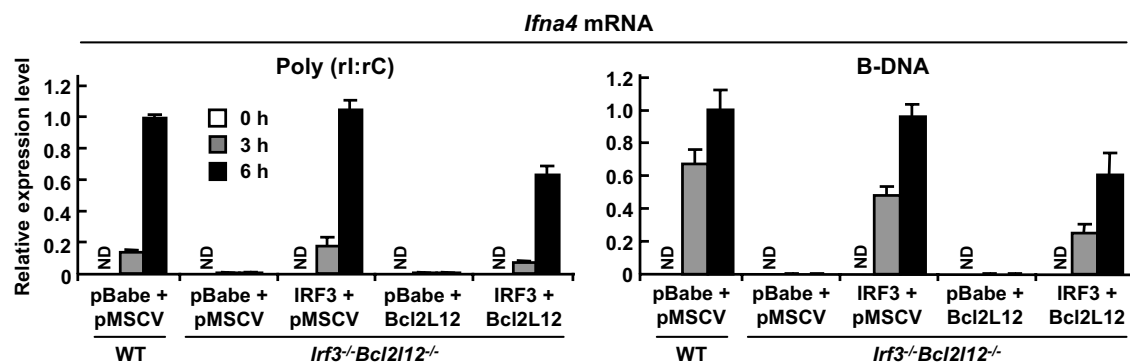
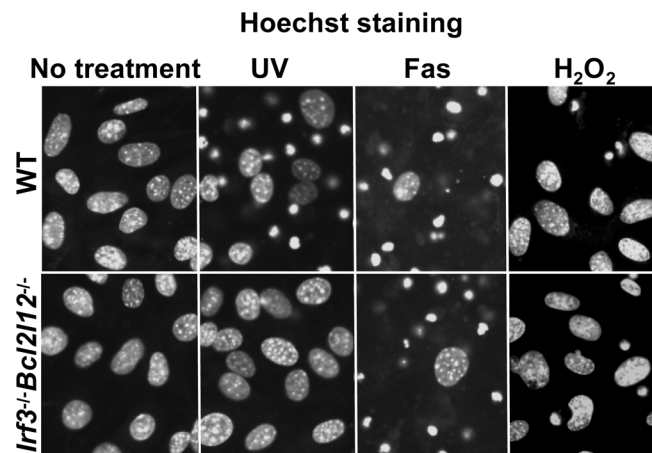


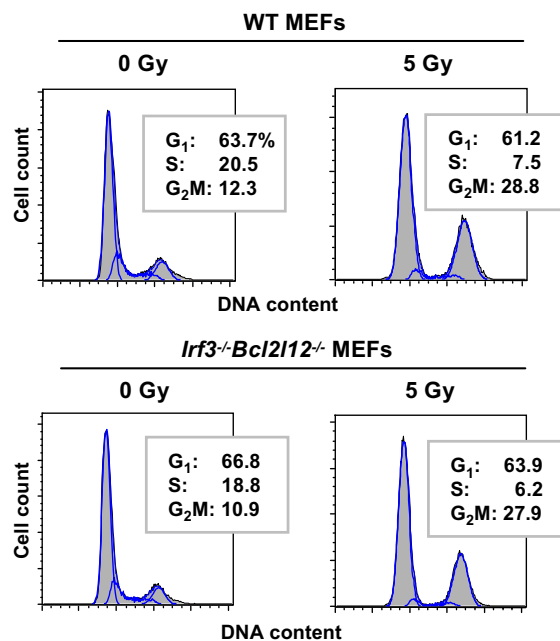
Fig. S2. Expression of transduced proteins. Western blot analysis was performed for HA-IRF3 and Bcl2L12-YFP using anti-HA and anti-GFP antibodies.



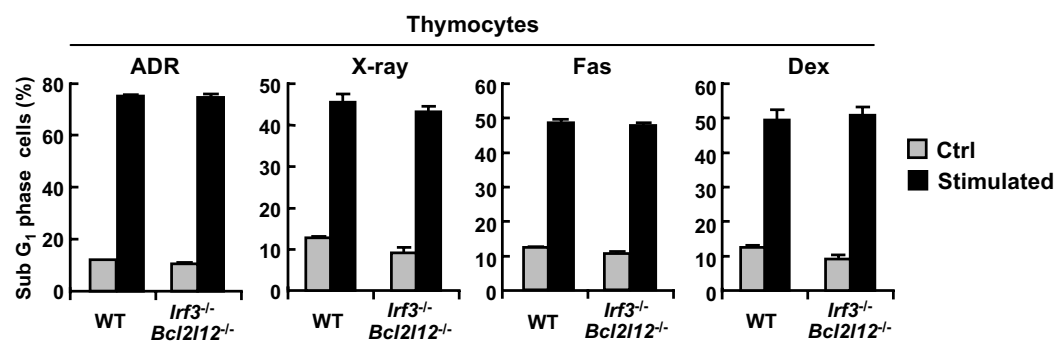
**Fig. S3.** qRT-PCR for *Ifna4* mRNA. WT and *Irf3*<sup>-/-</sup> *Bcl2L12*<sup>-/-</sup> MEFs transduced with HA-IRF3 and/or Bcl2L12-YFP were stimulated with poly(rI:rC) or B-DNA for the indicated periods as in Fig. 2, and *Ifna4* mRNA expression levels were measured by qRT-PCR.



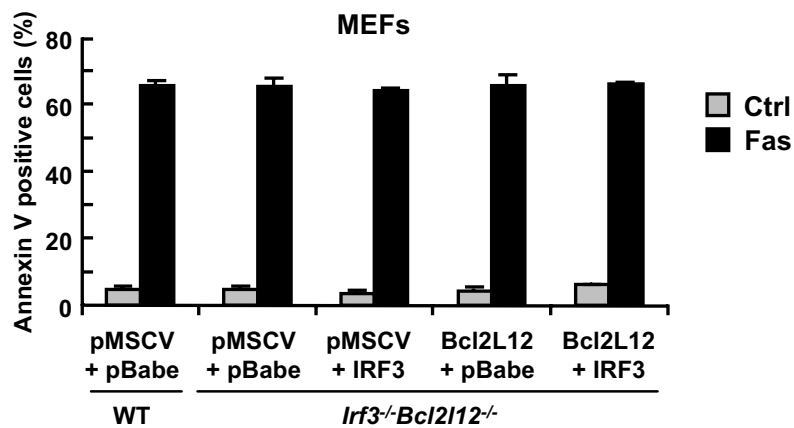
**Fig. S4.** Hoechst staining. MEFs from WT and *Irf3<sup>-/-</sup>Bcl2l12<sup>-/-</sup>* mice were treated as in Fig. 3A (Left) and stained with Hoechst 33342 at 18 h.



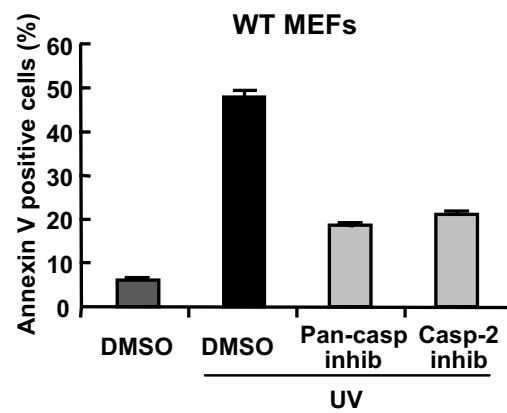
**Fig. S5.** Cell cycle arrest upon X-ray irradiation. Primary MEFs from WT and *Irf3<sup>-/-</sup>Bcl2/12<sup>-/-</sup>* mice were X-ray irradiated at 5 Gy, and then DNA content was measured 24 h after irradiation.



**Fig. 56.** Sensitivity to apoptotic stimuli in WT and *lrf3*<sup>-/-</sup>*Bcl2l12*<sup>-/-</sup> thymocytes. Cells from WT and *lrf3*<sup>-/-</sup>*Bcl2l12*<sup>-/-</sup> mice were treated with ADR (1  $\mu$ g/mL), X-ray (5 Gy), Fas (100 ng/mL Jo2 plus 100 ng/mL protein A) or Dex (1  $\mu$ M), and then subjected to DNA content analysis at 11 h. Data were reproduced in another independent experiment.



**Fig. S7.** Bcl2L12-independent apoptosis by Fas. Primary MEFs from WT and *lrf3*<sup>-/-</sup> *Bcl2l12*<sup>-/-</sup> mice were transduced with empty retrovirus, pBabeHA-IRF3 and/or pMSCV-Bcl2L12-YFP, treated with an agonistic Fas antibody for 18 h as in Fig. 3A, and stained with annexin V.



**Fig. S8.** The effect of caspase inhibitors on UV-induced apoptosis in MEFs. Primary MEFs from WT and *Irf3*<sup>-/-</sup> *Bcl2/12*<sup>-/-</sup> mice were UV irradiated in the absence or the presence of 50  $\mu$ M z-VAD-FMK (pan-caspase inhibitor) or 50  $\mu$ M z-VDVAD-FMK (caspase-2 inhibitor), and then stained with annexin V at 18 h.